

PCTWORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶: A01N 37/18, 43/04, C12Q 1/00, 1/02, 1/68, C12N 5/00, 5/06, 15/00, 15/06, 15/09, 15/10, 15/11, G01N 33/53	A2	(11) International Publication Number: WO 98/54963 (43) International Publication Date: 10 December 1998 (10.12.98)
(21) International Application Number: PCT/US98/11422 (22) International Filing Date: 4 June 1998 (04.06.98) (30) Priority Data: 60/048,915 6 June 1997 (06.06.97) US 60/048,882 6 June 1997 (06.06.97) US (Continued on the following page) (71) Applicant (for all designated States except US): HUMAN GENOME SCIENCES, INC. [US/US]; 9410 Key West Avenue, Rockville, MD 20850 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): YOUNG, Paul [US/US]; 122 Beckwith Street, Gaithersburg, MD 20878 (US). GREENE, John, M. [US/US]; 872 Diamond Drive, Gaithersburg, MD 20878 (US). FERRIE, Ann, M. [US/US]; 13203 L Astoria Hill Court, Germantown, MD 20874 (US). RUBEN, Steven, M. [US/US]; 18528 Heritage Hills Drive, Olney, MD 20832 (US). ROSEN, Craig, A. [US/US]; 22400 Rolling Hill Road, Laytonsville, MD 20882 (US). HU, Jing-Shan, [CN/US]; 1247 Lakeside Drive #3034, Sunnyvale, CA 94086 (US). OLSEN, Henrik, S. [DK/US]; 182 Kendrick Place #24, Gaithersburg, MD 20878 (US). EBNER, Reinhard [DE/US]; 9906 Shclburne Terrace #316,	<p>Gaithersburg, MD 20878 (US). BREWER, Laurie, A. [US/US]; 14920 Mt. Nebo Road, Poolesville, MD 20837 (US). MOORE, Paul, A. [GB/US]; Apartment 104, 1908 Holly Ridge Drive, McLean, VA 22102 (US). SHI, Yanggu [CN/US]; 437 West Side Drive, Gaithersburg, MD 20878 (US). FLORENCE, Charles [US/US]; (US). FLORENCE, Kimberly [US/US]; 12805 Atlantic Avenue, Rockville, MD 20851 (US). LAFLEUR, David, W. [US/US]; 1615 Q Street, N.W. #807, Washington, DC 20009 (US). NI, Jian [CN/US]; 5502 Manorfield Road, Rockville, MD 20853 (US). FAN, Ping [CN/US]; Apartment 302, 335 West Side Drive, Gaithersburg, MD 20878 (US). WEI, Ying-Fei [CN/US]; 13524 Straw Bale Lane, Darnestown, MD 20878 (US). FISCHER, Carrie, L. [US/US]; 5810 Hall Street, Burke, VA 22015 (US). SOPPET, Daniel, R. [US/US]; 15050, Stillfield Place, Centreville, VA 22020 (US). LI, Yi [CN/US]; 1247 Lakeside Drive #3034, Sunnyvale, CA 94086 (US). ZENG, Zhizhen [CN/US]; 13950 Saddleview Drive, Gaithersburg, MD 20878 (US). KYAW, Hla [MM/US]; 520 Sugarbush Circle, Frederick, MD 21703 (US). YU, Guo-Liang [CN/US]; 13524 Straw Bale Lane, Darnestown, MD 20878 (US). FENG, Ping [CN/US]; 4 Relda Court, Gaithersburg, MD 20878 (US). DILLON, Patrick, J. [US/US]; 1055 Snipe Court, Carlsbad, CA 92009 (US). ENDRESS, Gregory, A. [US/US]; 9729 Clagett Farm Drive, Potomac, MD 20854 (US). CARTER, Kenneth, C. [US/US]; 11601 Brandy Hall Lane, North Potomac, MD 20878 (US).</p> <p>(74) Agents: HOOVER, Kenley, K. et al.; Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, MD 10850 (US).</p> <p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SO, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p>Published With declaration under Article 17(2)(a); without abstract; title not checked by the International Searching Authority.</p>	
(54) Title: 207 HUMAN SECRETED PROTEINS		

AAAAGGTGTG TACAGGAGAT TTA CTGGCAA CTGTTCTTTT CCCATCAAAA ATCAGTGAAT 3300
 GTTTGCTGAG TATAAATGCT GCTTCCTTAA ACCACTTGTC GCTTTAGGAT CAACTTTACC 3360
 5 TGTACCTTTT CTCCTTTCTT CCCTTGCCAC CTCAGGTGCA AATCTGAACT CAGTGTCTGC 3420
 TTCTTCCATT TTCTCGTCTC TCTCCCTCTT TCCCCATTA TCCATATGAC ATTATTTTAC 3480
 10 TTCAAATGAC AGCATCAATC TTA AAAAGAT ATACATTAAA ACTAAGGAGT TTTT TAAAG 3540
 AAAGCCTGAA TAAGTTCCTT TCCCTGGTAA CTTTGAAAAG CAGTCAGAGT TGCTATATAG 3600
 ATATATGTGG CTCCTTTAAA ATGCTTTGTG TATGTGTGGT GTTTAAAAAA AAAAAAAAAA 3660
 15 TTCGGGGGGG GGCCCGGTNC CCAT 3684

20

(2) INFORMATION FOR SEQ ID NO: 116:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 1965 base pairs
 25 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 116:

30 AAGAAAGGGT ATTAAAATTC TAGATCACAT ATGGACCCGG GAAGGTTTPTT NACCCCTCTGT 60
 TAGTGACATC GAGTCTCCCA CTAGACAAAA TAGGTGGAAA AATCTCTCGA GGGCTCACAT 120
 35 TGTPTGTGCA TCTTCAGGAA AAACACCACC AGGCCATACC ACAGCCTGCC CAGTGAGGCG 180
 GTCTPTGCCA ACAGCACCCG GATGCTGGTG GTGGCCTTTG GGCTGCTGGT GCTCTACATC 240
 40 CTTCTGGCTT CATCTTGGAA GCGCCAGAG CCGGGATCC TGACCGACAG ACAGCCCTG 300
 CTGCATGATG GGGAGTGAAG CAGCAGGAAG GGGCTCCCAA GAGCTCCTGG TGGTCAGCC 360
 TGTGCTCCCC TCAGAAGCTC TGCTCTTCCC AGGCTCCCG GCTGGTTTCA GCAGGCGACT 420
 45 TTCTTCCAAT GCTGGGCCCA GACTTCTTGC CTGGGTGCTG GCCTGCCCTC TCCGNCCTGC 480
 TTGCTGCCCTG TCTGCTTTCC TTGGTGGVTT TGCTGGGTGC TGGGCCTGCC CTCTCCGGCC 540
 GCTTGCTGCC TGTCTGCTTT CCTTGGTGGC TTTGCTGGGT GCTGGGCCTG CCTTCTCTGG 600
 50 CTGCTTGCTG CTTGCTTGCT TTCTTGGTG GCTTGGCTT CTGCACTCCT TGGCGTCASC 660
 TCTCAGGTCC TCCATTACCA CGAGGTCTCT CTCGCTCTGG CCGCTCTTGC TGCTCTGTG 720
 55 TGAAGAWATC AGACTGATTT CCTCTAAGA CTCCTAGGGA TGTGGTGAAG AGCTGGGACT 780
 CAAGTGCACT CCACGGTGTG AAACATGAGG GARGTGAGGT GTCCCTCCAC TTCCCCCATA 840
 60 AAGGTGTGCA TTTCACTTAG GCTGCCCCGC CACAGAGCAG GCTTCATCTG CTCTGCCATC 900

CAGCCCCATC TGGATGTGAG GTGGGGTGA GACATCATGG GGTGATTGCA GAAAGGGGGA 960
 GTGGCGGCCC ACGCAGCTTC TGCTGAGGAG CTGACCGCTC TGAGCTGTTC TGTTTCGAT 1020
 5 TGCTGCTCTG TGCTGCGATG TATTGTGACC GTGGGGCTCC ACCTCTTCCA GCTGCTGCTA 1080
 CAGCTGAGGC CTGGATCCCG GCCTTTCCCT GTGACTTACG TGTCTGTAC CCGCANGCAG 1140
 CCCTACAAAT CCTGGTGACC TGCTCTCCA AGAACAGAGC CTGTCCCCAG ATGTCCAGT 1200
 10 AGCGATGAGT AACAGAGGTG GCTGTGGACT TCCTCTACTT CTCCTTGCTG GATCAGGGCC 1260
 TTCTGCTCTC CCGCTGGGCA GGTCTGGCCT TGCTCTCTG GCAGGGCCCC AGCCCTCTG 1320
 15 ACCACTCTGC AGCTACCAT GCAGCTGATG CCAAAGTTGT GGTGTCCAGT GTGCAGCAGC 1380
 CCTGGGAGCC ACTGCCACCT TCAGAGGGGT TCCTTGCTGA GACCCACATT GCTTCACCTG 1440
 GCCCCACCAT GGCTGCTTGC CTGGCCCAAC CTAGCGTTCT GTGCCATGCT AGAGCTTGAG 1500
 20 CTGTTGCTCT TCTTCAGGGG AGGAAATAGG GTGGAGAGCG GGAAGGGTCT TGCTCTAAG 1560
 TGTGCTGCT GTGGCTTTT TGCCTTCTCC AAAGACGCAC TGCCAGGTCC CAAGCTTCAG 1620
 25 ACTGCTGTGC TTAGTAAGCA AGTGAGAAGC CTGGGGTTTG GAGCCACCT ACTCTCTGGC 1680
 AGCATCAGCA TCCTACTCCT GGCAACATCA GGCCAACGTC CACCCAGCC TCACATTGCC 1740
 AGATGTTGGC AGAAGGGCTA ATATTGACCG TCTTGACTGG CTGGAGCCTT CAAAGCCACT 1800
 30 GGGATGTCCT CCAGGCACCT GGGTCCCAG ACCAGCTCCC CGTCTCCATA GGGGTAGGCA 1860
 TTTCAGTGGT TTAATGAAGCT CGAGTTTCAT TAAATATGTT AAGAATCAA GCTGTCTTTG 1920
 35 TTCAGGCTGC TATAACAAA ATATAATAGC CTGGGTGGCT TAAAC 1965

40 (2) INFORMATION FOR SEQ ID NO: 117:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 503 base pairs
 (B) TYPE: nucleic acid
 45 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 117:

50 AGTGATCCCC TTGCTCGGC CTCCCAAAAT GCTGGAATTG TAAGCGTGGG CCTCTGCACC 60
 CGGCCTGGTC CGCAATTTAA AAACGCACAG CCACCATTC CTYTCCAGAA AGCAGCCAGA 120
 TGCCTTTGGG AGAACCAGCC TCCTCCATGG AGGAAAGCTT GGGATCTGCC TTCCACCTG 180
 55 GGGAGGAGAG GGATCTGTGG AAAATCCTTC TGACGGACTT CCCCTCAGTG CCTGATCCAT 240
 ACTCAATAGT AGAAAAAGTA AGAAATATAC AAAGATAGCA GATACACGGA GACAGTTCCC 300
 60 CAAATAGCTG ACCGAWTAGC GCAGAAGCAA TATTGAAGAC CTAATAGCTG AGACATTTCC 360

What Is Claimed Is:

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:

(a) a polynucleotide fragment of SEQ ID NO:X or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;

(b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;

(c) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y or a polypeptide domain encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;

(d) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:Y or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;

(e) a polynucleotide encoding a polypeptide of SEQ ID NO:Y or the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X, having biological activity;

(f) a polynucleotide which is a variant of SEQ ID NO:X;

(g) a polynucleotide which is an allelic variant of SEQ ID NO:X;

(h) a polynucleotide which encodes a species homologue of the SEQ ID NO:Y;

(i) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(h), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues.

2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding a secreted protein.

3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO:Y or the polypeptide encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X.

4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises the entire nucleotide sequence of SEQ ID NO:X or the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X.
5. The isolated nucleic acid molecule of claim 2, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.
6. The isolated nucleic acid molecule of claim 3, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.
7. A recombinant vector comprising the isolated nucleic acid molecule of claim 1.
8. A method of making a recombinant host cell comprising the isolated nucleic acid molecule of claim 1.
9. A recombinant host cell produced by the method of claim 8.
10. The recombinant host cell of claim 9 comprising vector sequences.
11. An isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:
 - (a) a polypeptide fragment of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
 - (b) a polypeptide fragment of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z, having biological activity;
 - (c) a polypeptide domain of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
 - (d) a polypeptide epitope of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
 - (e) a secreted form of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
 - (f) a full length protein of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;

- (g) a variant of SEQ ID NO:Y;
 - (h) an allelic variant of SEQ ID NO:Y; or
 - (i) a species homologue of the SEQ ID NO:Y.
12. The isolated polypeptide of claim 11, wherein the secreted form or the full length protein comprises sequential amino acid deletions from either the C-terminus or the N-terminus.
13. An isolated antibody that binds specifically to the isolated polypeptide of claim 11.
14. A recombinant host cell that expresses the isolated polypeptide of claim 11.
15. A method of making an isolated polypeptide comprising:
- (a) culturing the recombinant host cell of claim 14 under conditions such that said polypeptide is expressed; and
 - (b) recovering said polypeptide.
16. The polypeptide produced by claim 15.
17. A method for preventing, treating, or ameliorating a medical condition, comprising administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim 11 or the polynucleotide of claim 1.
18. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:
- (a) determining the presence or absence of a mutation in the polynucleotide of claim 1; and
 - (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of said mutation.
19. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:
- (a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample; and
 - (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

20. A method for identifying a binding partner to the polypeptide of claim 11 comprising:

- (a) contacting the polypeptide of claim 11 with a binding partner; and
- (b) determining whether the binding partner effects an activity of the polypeptide.

21. The gene corresponding to the cDNA sequence of SEQ ID NO:Y.

22. A method of identifying an activity in a biological assay, wherein the method comprises:

- (a) expressing SEQ ID NO:X in a cell;
- (b) isolating the supernatant;
- (c) detecting an activity in a biological assay; and
- (d) identifying the protein in the supernatant having the activity.

23. The product produced by the method of claim 22.